Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Acceptability for Continuing Registration

PACR2007-01

Re-evaluation of S-methoprene

The purpose of this document is to inform registrants, pesticide regulatory officials and the Canadian public that Health Canada's Pest Management Regulatory Agency (PMRA) has re-evaluated S-methoprene. The PMRA has determined that S-methoprene is acceptable for continued registration with the implementation of additional mitigation measures to further protect workers and the environment. Registrants will be required to submit specified data. Upon finalization of the re-evaluation decision, the PMRA will provide registrants of products containing S-methoprene with specific direction on how to address these measures and requirements.

This Proposed Acceptability for Continuing Registration (PACR) document provides a rationale for the proposed regulatory decision for S-methoprene. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications at the address below.

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Table of Contents

1.0 Background 1

2.0 Re-evaluation of S-methoprene 1
- 2.1 Identification 2
- 2.2 Description of Uses 3
- 2.3 Effects Having Relevance to Human Health 3
- 2.4 Environmental Assessment 3
  - 2.4.1 Environmental Fate 4
  - 2.4.2 Environmental Toxicology 5
  - 2.4.3 Concentrations in Drinking Water 6
  - 2.4.4 Terrestrial Risk Assessment 6
  - 2.4.5 Aquatic Risk Assessment 7
  - 2.4.6 Canadian Considerations 8
  - 2.4.7 Environmental Assessment Conclusions 9
  - 2.4.8 Environmental Risk Mitigation 9

3.0 Proposed Re-evaluation Decision 9

4.0 Proposed Regulatory Actions 9
- 4.1 Proposed Canadian Regulatory Actions Relating to Human Health 10
- 4.2 Proposed Regulatory Actions Relating to Environment 10
- 4.3 Maximum Residue Limits 11

5.0 Additional Data Requirements 11

6.0 Supporting Documentation 11

Appendix I Products Containing S-methoprene Registered in Canada as of 28 April 2005 . 13

1.0 Background

The PMRA is re-evaluating all pesticides, both active ingredients and formulated end-use products, that were registered prior to 31 December 1994 to ensure that their continued acceptability is examined using current scientific approaches. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

S-methoprene has been re-evaluated by the PMRA under Re-evaluation Program 1 as described in DIR2001-03. Under Program 1, the PMRA relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents, to assess Canadian pest control products. For products to be re-evaluated under Program 1, there must exist a suitable foreign review that meets the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian regulatory decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Based on the outcome of foreign reviews, the PMRA will propose, under Program 1, a regulatory decision and appropriate mitigation measures for Canadian uses of an active ingredient.

The USEPA conducted a re-evaluation of methoprene (racemate of R- and S-methoprene) and concluded that, on the basis of health and environmental risk assessments, it was eligible for reregistration with implementation of mitigation measures. These conclusions were published in a 1991 RED document for methoprene; a 1991 methoprene RED Fact Sheet; a June 2001 updated methoprene RED Fact Sheet; and in the Inert Ingredient Focus Group Decision Document on Tolerance Reassessment for Methoprene published in August 2002. In its re-evaluation of S-methoprene, the PMRA based its conclusions on these documents taking into account the Canadian use pattern and issues (e.g., the federal Toxic Substances Management Policy [TSMP]). In addition to the USEPA documents, the PMRA environmental assessment used information from the United Kingdom (UK) Advisory Committee on Pesticides, the New Zealand Report for the Ministry of Health, published literature and toxicology websites. A review of the chemistry of Canadian products was also conducted.

2.0 Re-evaluation of S-methoprene

In Canada, methoprene R- and S-methoprene was first registered in 1982. According to current end-use product labels, this active ingredient is registered in Canada to control insect pests in mushroom cultures and stored tobacco as well as fleas and ticks on dogs, cats and indoor premises. It is also used to prevent the emergence of adult mosquitoes from standing water including flood water sites, permanent water sites, storm drain ditches and roadside ditches. Canadian products containing S-methoprene are listed in Appendix I.

Based on the comparison of American and Canadian use patterns, the USEPA assessment described in the RED document for methoprene is considered to be an adequate basis for the proposed Canadian re-evaluation decision for human health for S-methoprene. The details of the assessments conducted by the USEPA are presented in the RED for methoprene. An environmental assessment for S-methoprene was conducted by the PMRA with emphasis on use as mosquito larvicide in Canadian environment and was based on USEPA, UK and New Zealand documents as well as other documents on methoprene or S-methoprene.

The federal Toxic Substances Management Policy and Regulatory Directive DIR99-03 were taken into consideration during the review of S-methoprene, and it was concluded that S-methoprene is not a candidate for Track 1 classification. The technical product is not expected to contain impurities of toxicological concern as identified in Regulatory Directive DIR98-04 or TSMP Track 1 substances as identified in Appendix II of DIR99-03.

2.1 Identification of the Active Substance

Active substance: S-methoprene

Function: Insect growth regulator

Chemical names:

IUPAC: isopropyl (E,E)-(S)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate

CAS: 2,4-dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, 1-methylethyl ester, (2E,4E,7S)

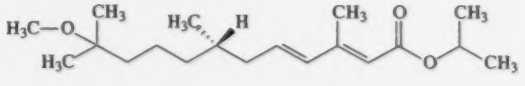
Chemical class: methyl alkyldienoate

CAS number: 65711-16-6

Molecular formula: $C_{19}H_{34}O_3$

Molecular weight: 310.5

Structural formula:



Registration number: 21191

Purity (nominal): 94.0% (limits 91.0– 98.7%)

2.2 Description of Uses

In Canada, S-methoprene is registered for the control of insect pests in mushroom culture and stored tobacco, fleas and ticks on dogs, cats and indoor premises, as well as to prevent the emergence of adult mosquitoes from the following sites:

- standing water, including flood water sites (pasture, meadows, marches, swamps, snow pools, woodland pools, etc.);
- permanent water sites (ornamental ponds and fountains, flooded crypts, construction and other man made depressions, tree holes, other artificial water holding containers);
- storm drain ditches; and
- roadside ditches.

In Canada, the majority of domestic products are registered for use to prevent emergence of adult fleas on dogs and cats and include aerosol spray, liquid spray, shampoo, application tube and pet collar. Ten domestic and one commercial products packaged as pressurized and non-pressurized liquid formulations are registered for use to prevent the emergence of fleas and ticks in indoor premises (carpet, furniture and other household items). Other commercial products formulated as emulsifiable concentrate and solution are registered for use in mushroom culture or stored tobacco.

Three restricted products, packaged as pellets, granules and briquettes are registered for use to prevent the emergence of adult mosquitoes in flood water sites and permanent water sites.

2.3 Effects Having Relevance to Human Health

The USEPA conducted a re-evaluation of methoprene and concluded that, on the basis of health and environmental risk assessments, it was eligible for reregistration. These conclusions were published in the RED for methoprene and subsequent documents. These documents addressed uses of methoprene that are also registered in Canada. With respect to human health, the PMRA has determined that the USEPA assessments included in these documents represent an adequate basis for the proposed Canadian re-evaluation decision. The Canadian registrants are required to modify labels of end-use products as outlined in Section 4.1 of this PACR.

2.4 Environmental Assessment

The environmental assessment of S-methoprene is limited to application as a mosquito larvicide and does not include applications for control of insect pests on domestic pets, or in mushroom culture and stored tobacco, because these uses are mainly indoors and have limited potential for environmental exposure.

This review is based on foreign reviews on methoprene from the USEPA RED, the updated USEPA RED and reviews on S-methoprene from the United Kingdom Advisory Committee on Pesticides, the New Zealand Report for the Ministry of Health (on S-methoprene), the published literature and toxicology websites.

A refined approach to calculate the expected environmental concentrations (EECs) in water was conducted for the granular, pellet and briquet formulations of mosquito larvicide. Product data were reviewed, as there is only one product registered of each formulation (trademark Altosid). This review takes into consideration the slow release of the active ingredient from the formulations by factoring in the current label recommendations on the length of time the product is effective, the half-life ($t_{1/2}$) in pond water and the maximum application rates. For the briquet formulation, the EEC calculation of methoprene was based on the recommendation of the number of briquets to be added according to the volume of water of the catch basin. This method assumes that methoprene is released at a constant rate from these products and provides a good estimate of the concentration of methoprene in water after application.

In assessing the environmental risk of methoprene, a deterministic approach was used. In this standard PMRA approach, risk was characterized by the quotient method, the ratio of the EEC to the effects endpoint of concern. Risk quotient (RQ) values less than one are considered indicative of a low risk of non-target effects occurring, whereas values greater than one are considered to indicate that some degree of risk exists for effects on non-target organisms.

The effects endpoints included both acute and chronic, chosen from the range of toxicity tests on species available. Effects endpoints, chosen from the most sensitive species, were used as surrogates for the wide range of species that can be potentially exposed following treatment with methoprene.

2.4.1 Environmental Fate

The physico-chemical properties of R-S and S-methoprene are fairly similar. The solubility of methoprene varied from being sparingly soluble for S-methoprene (0.5 mg/L) to low for the racemate (1.4 mg/L). Both forms have a vapour pressure of (2.37×10^{-5} mm Hg) that is intermediate to high. Henry's law constant (1.26×10^{3}– 3.53×10^{3}) indicates slight volatility from water or moist surfaces. The partition coefficient (log K_{ow}: 4.6–5.3) indicates the potential for bioaccumulation.

Methoprene is not susceptible to hydrolysis ($t_{1/2} > 4$ weeks) in buffered solutions at pH 5, 7 or 9. Photolysis and biotransformation are the most important processes affecting the transformation of methoprene in both the aquatic and terrestrial environments. Methoprene is highly susceptible to photolysis with photolytic $t_{1/2}$s in water of 4–5 days, classifying it as non-persistent. Data from a study indicated that when methoprene in water was exposed to sunlight, it undergoes photoisomerization with a $t_{1/2}$ of about 30 minutes. In pond water, methoprene is non-persistent ($t_{1/2}$s ranged from 30 to 40 h).

No abiotic transformation studies were available on soil; however, on inert surfaces (glass) methoprene had a photolytic $t_{1/2}$ of six hours. Methoprene is non-persistent in soil primarily due to aerobic biotransformation with reported field $t_{1/2}$ up to 14 days. The major transformation product is carbon dioxide. Soil adsorption studies show that methoprene is quickly adsorbed to sandy loam soils and is classified as slightly mobile (K_d 33.5). Leaching studies showed that methoprene residues are primarily restricted to the top few centimetres of soils in both laboratory

and field studies. It will therefore not leach. Combined with rapid biotransformation in soil, methoprene should not persist in soil or contaminate groundwater.

2.4.2 Environmental Toxicology

2.4.2.1 Terrestrial

Methoprene showed no immediate acute effects on adult honeybees, as their mortality after 48 h did not exceed 10% after topical or oral application of the doses tested (up to 1000 µg/bee). At 250 µg/bee, some studies have shown behavioural changes, developmental abnormalities and disruption of hormonal regulation over periods ranging from 1 to 21 days. These effects were not seen at 25 µg/bee. Earthworms showed little if any toxic effects to methoprene exposure. Methoprene is practically non-toxic to mallard ducks and bobwhite quail on both an oral and dietary basis (lethal dose 50% [LD_{50}] > 2000 mg/kg, lethal concentration 50% [LC_{50}] > 10 000 mg/kg). Acute LD_{50}s for rats and dogs range from 5000 to 34 600 mg a.i./kg; therefore, methoprene is classified as being practically non-toxic. Mammal dietary NOELs range from 20 to 250 mg/kg bw/day. Methoprene showed little phytotoxicity to flowering plants, peas and tomatoes.

2.4.2.2 Aquatic

Acute Toxicity

Methoprene is very highly toxic to *Daphnia magna* (24–72 h LC_{50}s range from 0.002 to 0.09 mg a.i./L). The 5-day lethal time 50% (TL_{50}), comparable to LC_{50}, for crayfish ranged from 0.46 to > 10.0 mg a.i./L, classifying methoprene as slightly toxic to highly toxic. Methoprene is highly toxic to aquatic sowbugs *Aselleus hilgendorfi* (48 h LC_{50}: 0.03 mg a.i./L) and moderately toxic to bladder snail *Physa fontinalis* (48 h LC_{50}: 1.06 mg a.i./L). Methoprene is highly toxic to diving beetles (*Laccophilus sp.*), backswimmers (*Notonecta unifasciata*) and water boatmen (*Corisella decolor*); 24–96 h LC_{50}s range from 0.12 to 0.20 mg a.i./L for these organisms. When exposed to S-methoprene for 24 h and 48 h, LC_{50}s for *Moina macrocopa* are 0.51 and 0.34 mg a.i./L, respectively. Methoprene is highly toxic to this species.

Data on toxicity to fish were available on both methoprene and S-methoprene and indicated a range of toxicity endpoints. Methoprene is moderately to highly toxic to bluegill sunfish (*Lepomis macrochirus*) (96 h LC_{50}s range from 0.105 to 4.40 mg a.i./L). Available data showed that methoprene exhibits a wide range of toxicities to rainbow trout (*Onchorhynchus mykiss*), as 96 h LC_{50}s ranged from 0.439 to 106 mg a.i./L, classifying it as practically non-toxic to highly toxic. S-methoprene is highly toxic to rainbow trout (96 h LC_{50}: 0.76 mg a.i./L). Methoprene is practically non-toxic to Channel catfish (*Ictalurus punctatus*) (96 h LC_{50}: > 100 mg a.i./L), moderately toxic to fathead minnows (*Pimephales promelas*) (96 h LC_{50}: > 10 mg a.i./L) and slightly toxic to Coho salmon (*Onchorhynchus kisutch*) (96 h LC_{50}: 86 mg a.i./L).

In the marine/estuarine environment, S-methoprene is classified as highly toxic to the Mysid shrimp *Mysidopsis bahia* (96 h LC_{50}s: < 0.13 mg a.i./L, 96 h no observed effect concentration (NOEC): 0.062 mg a.i./L). Methoprene is moderately to highly toxic to various life stages of the

copepod *Apocyclops spartinus* (48 h LC_{50}s range: from 0.8 to > 10 mg a.i./L). The 24–96 h LC_{50}s for *Gammarus aequicauda* range from 0.21 to 1.41 mg a.i./L, classifying methoprene as moderately to highly toxic to the scud. Five-day LC_{50}s for the blue crab and salt water shrimp were both > 10.0 mg a.i./L.

Chronic Toxicity

A 17-day NOEC of 0.01 mg a.i./L was determined in a chronic toxicity study of S-methoprene to the water flea *Moina macrocopa*. The lowest observed effect concentration (LOEC) was 0.05 mg a.i./L, based on longevity, reproductive capacity and population growth. Little data is available to determine the chronic effect of methoprene to fish. The 37-day NOEC and LOEC for newly spawned fathead minnows, *Pimephales promelas*, based on analyses of fry length and weight, were 0.048 and 0.084 mg a.i./L, respectively. Populations of the mosquito fish *Gambusia affinis*, exposed to methoprene in experimental ponds for a five-month period resulted in no visible adverse effect on the fish after 5 applications of 0.034 kg a.i./ha at monthly intervals.

In the marine environment, the 20- and 8-day LC_{50}s for daggerblade grass shrimp (*Palaeomontes pugio*) are 0.062 and 0.125 mg/L, respectively. A 40-day NOEC of > 0.20 mg a.i./L was also determined. No adverse effects on the crabs (*Uca pugilator*) time to 2nd moulting or number of crabs that moulted were observed at 0.02 mg a.i./L over 40 days. Time to moult was also not affected in *P. pugio* when exposed to 0.2 mg a.i./L. Mysid shrimp (*Mysidopsis bahia*) is very sensitive to technical S-methoprene at concentrations as low as 0.002 mg a.i./L. Twenty-six day NOECs for survival, mean day of brood release, total production of young in first brood and number of young produced per female were 0.062, 0.002, 0.004 and < 0.002 mg a.i./L, respectively. The 49-day NOEC and LOEC for Mysid shrimp growth were < 0.052 and 0.099 mg a.i./L, respectively. The mud crab exposed for 4 weeks to 6 different S-methoprene concentrations had LOEC and NOECs for survival of 0.10 and 0.01 mg a.i./L, respectively, for two separate life stages (hatch to megalops and megalops to crab).

2.4.3 Concentrations in Drinking Water

Methoprene is expected to have limited impact on drinking water sources in Canada due to its susceptibility to photolysis and biotic transformation. Application of sustained-release formulations to water will result in continued release of methoprene. However, methoprene once released is not persistent in the water column and would be preferentially adsorbed to organic matter. The USEPA RED indicates that by the time surface water reaches drinking water treatment plants, residues of methoprene are unlikely to be present and in the unlikely event that residues are present, these would be mitigated by water treatment procedures.

2.4.4 Terrestrial Risk Assessment

In view of the limited potential for terrestrial exposure, there was no environmental risk assessment conducted on the terrestrial use patterns, which are mainly indoor.

2.4.5 Aquatic Risk Assessment

2.4.5.1 Acute Toxicity

For both the Altosid granule and pellet formulations, freshwater aquatic invertebrates (*Moina macrocopa*) show low acute risk (RQ = 0.41) from the expected concentrations of methoprene. Freshwater fish (*Onchorhynchus mykiss*) also show low acute risk (RQ = 0.18) as do marine invertebrates (*Mysidopsis bahia*) (RQ = 0.23). The Altosid XR Briquet formulation shows low acute risk to freshwater aquatic invertebrates (RQ = 0.15), negligible risk to both freshwater fish (RQ = 0.07) and marine invertebrates (RQ = 0.08).

2.4.5.2 Chronic Toxicity

For both the Altosid granule and pellet formulations, freshwater invertebrates (*Moina macrocopa*) show moderate risk (RQ = 1.40) to methoprene on a chronic basis. Freshwater fish (*Pimephales promelas*) show a low risk (RQ = 0.29) and marine invertebrates (*Mysidopsis bahia*) show moderate risk (RQ = 7.0) to methoprene. The Altosid XR Briquet formulation shows low chronic risk to freshwater aquatic invertebrates (RQ = 0.50) and freshwater fish (RQ = 0.10) and moderate risk to marine invertebrates (RQ = 2.50).

2.4.5.3 Marine Life-Cycle Chronic Toxicity

Ecological concerns were identified in the 1991 methoprene RED Facts (USEPA 1991) document relating to chronic toxicity to estuarine invertebrates were addressed when an estuarine invertebrate life cycle toxicity study was submitted to the USEPA in 1996. The submitted study indicated minimal chronic risk to Mysid shrimp, and as a result a label advisory statement regarding toxicity to estuarine organisms was removed from the American label by the USEPA.

2.4.5.4 Field Studies

Field studies with methoprene formulations have shown that there are no lasting adverse effects on populations of aquatic invertebrates or other non-target aquatic organisms when methoprene is used for mosquito control. Where negative impacts on some aquatic invertebrates were observed, they were not permanent as these communities recovered.

2.4.5.5 Incident Reports

Lobster Die-offs

Methoprene was suspected as a causative agent of a lobster die-off in Long Island Sound in 1999. The cause or causes of this die-off are presently not well understood. Multiple factors are suspected, including the aerial application of the mosquito adulticide malathion or the use of methoprene in catch basins. However, researchers have been sceptical of the pesticide theory, noting that while the lobster die-off peaked in the fall of 1999, it began in 1998, the summer before pesticide spraying began.

Beginning in 2001, research on lobster health and the factors affecting the Long Island Sound lobster population has been conducted by various university and government agencies in an attempt to determine the cause or causes of the 1999 lobster die-off. University of Connecticut and Stony Brook University, New York research scientists and biologists are currently working on the possible link between lobster deaths and pesticides. At present, only interim reports published on the Internet are available. Other research is being conducted on disease-causing organisms, pollution, lobster crowding, water quality conditions including elevated temperatures and changes in salinity as well as on environmental conditions such as storm events.

Frog Deformations

The discovery of deformed frogs in Minnesota began a controversy involving the widespread use of methoprene and other chemical pesticides as the causative agent of the observed deformations.

In one laboratory study, methoprene was directly implicated in hindleg deformities in emerging African Clawed frog (*Xenopus laevis*) when photolytic transformation products of methoprene (similar in structure to retinoids) were added to rearing water containing tadpoles. However, others have not been able to reproduce these results and have raised doubts of methoprene's contribution to the observed effects. In addition, there was a lack of geographic connection between methoprene use and the deformities observed in the field; the level of exogenous retinoids needed to produce a duplicated limb in a frog was extremely high (1700–15 000 times the normal application rate for methoprene); other studies have been unable to reproduce the most commonly seen malformations such as supernumary limbs, skin webbings and missing legs. Also, the type of deformities observed should be found in other amphibians and other aquatic organisms. Moreover, a recent study of methoprene by the USEPA concluded that methoprene does not cause frog deformities.

Currently, there is greater evidence that recent increases in malformations in amphibians may be due to increases in exposure to unsafe levels of UV light, increases in the rate of amphibian infection by parasitic trematodes and predation by other aquatic organisms such as leeches, small fish, insect larvae and other invertebrate predators.

2.4.6 Canadian Considerations

The PMRA has taken into account the federal Toxic Substances Management Policy during its review of methoprene. It has been determined that methoprene does not meet TSMP Track 1 criteria. Although the log octanol-water partition coefficient (log K_{ow}) ranges from 4.6 to 5.3, which is within the TSMP Track 1 cut-off criterion of log $K_{ow} \geq 5.0$, methoprene is not bioaccumulative (bioconcentration factors in fish range from 457 to 950). In addition, elimination of 93–95% of methoprene residues within 14 days precludes bioaccumulation of methoprene in fish. Methoprene does not meet the criteria for persistence as its $t_{1/2}$ values in water and soil are below the TSMP Track 1 cut-off criteria.

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2004-01, *Formulants Program*, published on 9 January 2004.

2.4.7 Environmental Assessment Conclusions

Assessment of the slow release formulations of methoprene for use as a mosquito larvicide has shown no more than a low acute risk to freshwater and marine invertebrates and freshwater fish. The chronic risk is moderate to aquatic invertebrates and low to fish. This use of methoprene does not pose an unacceptable risk to non-target aquatic organisms.

2.4.8 Environmental Risk Mitigation

The environmental risk associated with methoprene use as a mosquito larvicide is associated with its slow rate of action on the target mosquito larvae and the subsequent potential desire of the applicator to reapply due to lack of perceived effect. However, the granular, pellet and briquet formulations of methoprene are classified as "Restricted", because their use involves the direct application to water. Use of the products is limited to public health officials, mosquito abatement officials and other trained personnel of public mosquito programs. Therefore, the applicators' experience and knowledge should mitigate this tendency to reapply prematurely.

3.0 Proposed Re-evaluation Decision

The USEPA published a RED document for methoprene addressing the main science areas that are necessary for Canadian regulatory decisions, i.e., human health and the environment. This document addressed uses of S-methoprene that are also registered in Canada. The PMRA has determined that S-methoprene is acceptable for continued registration provided that the mitigation measures specified in Section 4.0 of this document are adopted. Additional data requirements are identified in Section 5.0.

It should be noted that for end-use products containing more than one active ingredient under re-evaluation, the registration status might change as a result of the re-evaluation of the remaining affected active ingredients.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision. Registrants of products containing S-methoprene should not apply for label amendments or submit the additional data as described in Section 5.0 during this comment period; they will be informed by letter of the specific instructions for addressing label changes and data requirements once the re-evaluation decision has been finalized.

4.0 Proposed Regulatory Actions

Canadian end-use product labels should be amended to include the following statements to further protect users and the environment. A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

4.1 Proposed Canadian Regulatory Actions Relating to Human Health

1. For all domestic end-use products registered for use on cats and dogs, labels must comply with PMRA's current requirements as specified in Regulatory Directive DIR2002-01, *Canadian Label Improvement Program for Pesticides Used on Companion Animals*.

2. For commercial end-use products used on mushroom and tobacco, the following statement must be added to a section entitled **PRECAUTIONS**:

   - Wear chemical resistant gloves when handling and/or applying this product.

3. For restricted end-use products formulated as granules and pellets, the following statement must be added to a section entitled **PRECAUTIONS**:

   - Wear a NIOSH/MSHA-approved respirator during mixing/loading, clean-up and repair activities.

   - Wear chemical-resistant gloves when handling and/or applying this product.

4.2 Proposed Regulatory Actions Relating to Environment

1. For all products that are applied directly to water (i.e., all Altosid formulations), include the following statement on labels:

   - TOXIC to aquatic organisms.

2. For Altosid XR Briquets (Reg. No. 27694) change the following label statement:

   a)
   - From: *"Apply ALTOSID XR BRIQUETS early in the mosquito season, when larvae start to develop. Monitor larval populations to determine if and when further applications are required."*

   - To: *"Apply ALTOSID XR BRIQUETS early in the mosquito season, when larvae start to develop. The limit is one application per season, unless briquets have been flushed away."*

   b)
   - From: *"Large water flows may accelerate the dissolution of the briquet. Monitor larval populations to determine if and when further applications are required."*

   - To: *"Large water flows may accelerate the dissolution of the briquet. The limit is one application per season, unless briquets have been flushed or dissolved away."*

3. For Apex EC Insect Growth Regulator (Reg. No. 17247), include the following label statements:

   - DO NOT allow effluent or runoff from greenhouses or mushroom houses containing this product to enter lakes, streams, ponds or other waters.

   - TOXIC to aquatic organisms.

4.3 Maximum Residue Limits

There are no dietary concerns regarding the use of S-methoprene on food crops reported in the USEPA RED. This document adequately addresses the Canadian dietary exposure. S-methoprene is currently registered in Canada for use on mushrooms. S-methoprene may be used on other crops in other countries. Currently, maximum residue limits (MRLs) of S-methoprene and its metabolites must not exceed 0.1 ppm, a general MRL specified in Regulation B.15.002(1) of the Canadian Food and Drug Regulations. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2003-01, *Revocation of the 0.1 ppm General maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*.

5.0 Additional Data Requirements

The technical registrant of S-methoprene will be required to submit the following within 24 months of finalization of the re-evaluation decision:

- available water monitoring data on concentrations of methoprene in aquatic habitats, resulting from the mosquito larvicide use.

6.0 Supporting Documentation

PMRA documents, such as DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document *Methoprene* is available on the Office of Pesticide Programs' website at www.epa.gov/pesticides/reregistration under Chemical Status.

The USEPA RED Facts (*Methoprene*) is available on the Office of Pesticide Programs' website at www.epa.gov/oppsrrd1/REDs/factsheets/0030fact.pdf

The Code of Federal Regulation (40CFR186.4150; 1 July 1999) is available at www.gpoaccess.gov/cfr/retrieve.html

June 2001 Update of the March 1991 Methoprene RED. The fact sheet is available on the Office of Pesticide Programs' website at www.epa.gov/pesticides/biopesticides/ingredients/factsheets/factsheet_105401.pdf

The USEPA IIFG Decision Document on Tolerance Reassessment for Methoprene (1 August 2002)

The USEPA Federal Register (68FR34825-34929; 11 June 2003), Methoprene, Watermelon Mosaic Virus-2 Coat Protein, and Zucchini Yellow Mosaic Virus Coat Protein; Final Tolerance Actions

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Appendix I Products Containing S-methoprene Registered in Canada as of 28 April 2005

Product Name	Registrant	Registration Number	Guarantee (% a.i.)	Marketing Class
Apex EC Insect Growth Regulator	Wellmark International	17247*	Methoprene = 67	Commercial
Kabat Tobacco Protector	Wellmark International	17324	(S)-Methoprene = 5.2	Commercial
Precor Insect Growth Regulator	Wellmark International	21191	(S)-Methoprene = 94.0	Technical active ingredient
Vet-Kem Ovitrol Plus for dogs and cats (with Precor)	Wellmark International	21206	(S)-Methoprene = 0.27 Pyrethrins = 0.20 Piperonyl butoxide, technical = 0.37 N-octyl bicycloheptene dicarboximide = 0.62	Domestic
Vet-Kem Siphotrol P.M. (kills fleas)	Wellmark International	21357	(S)-Methoprene = 0.015 Pyrethrins = 0.20 Piperonyl butoxide, technical = 1.0 N-octyl bicycloheptene dicarboximide = 1.0	Domestic
Precor EC Emulsifiable Concentrate	Wellmark International	21573	(S)-Methoprene = 1.2	Commercial
Zodiac Flea & Tick Spray for Dogs and Cats	Wellmark International	21744	(S)-Methoprene = 0.27 Pyrethrins = 0.20 Piperonyl butoxide, technical = 0.37 N-octyl bicycloheptene dicarboximide = 0.62	Domestic
Zodiac Household Flea Spray	Wellmark International	21761	(S)-Methoprene = 0.015 Pyrethrins = 0.20 Piperonyl butoxide, technical = 1.0 N-octyl bicycloheptene dicarboximide = 1.0	Domestic

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Product Name	Registrant	Registration Number	Guarantee (% a.i.)	Marketing Class
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Kabat Tobacco Protector	Wellmark International	17324	(S)-Methoprene = 5.2	Commercial
Precor Insect Growth Regulator	Wellmark International	21191	(S)-Methoprene = 94.0	Technical active ingredient
Vet-Kem Ovitrol Plus for dogs and cats (with Precor)	Wellmark International	21206	(S)-Methoprene = 0.27 Pyrethrins = 0.20 Piperonyl butoxide, technical = 0.37 N-octyl bicycloheptene dicarboximide = 0.62	Domestic
Vet-Kem Siphotrol P.M. (kills fleas)	Wellmark International	21357	(S)-Methoprene = 0.015 Pyrethrins = 0.20 Piperonyl butoxide, technical = 1.0 N-octyl bicycloheptene dicarboximide = 1.0	Domestic
Precor EC Emulsifiable Concentrate	Wellmark International	21573	(S)-Methoprene = 1.2	Commercial
Zodiac Flea & Tick Spray for Dogs and Cats	Wellmark International	21744	(S)-Methoprene = 0.27 Pyrethrins = 0.20 Piperonyl butoxide, technical = 0.37 N-octyl bicycloheptene dicarboximide = 0.62	Domestic
Zodiac Household Flea Spray	Wellmark International	21761	(S)-Methoprene = 0.015 Pyrethrins = 0.20 Piperonyl butoxide, technical = 1.0 N-octyl bicycloheptene dicarboximide = 1.0	Domestic

Product Name	Registrant	Registration Number	Guarantee (% a.i.)	Marketing Class
Altosid Pellets Mosquito Growth Regulator	Wellmark International	21809	(S)-Methoprene = 4.25	Restricted
Vet-Kem Siphotrol Forte Double Action	Wellmark International	22213	(S)-Methoprene = 0.01 Permethrin = 0.25	Domestic
Altosid Granules	Wellmark International	22676	(S)-Methoprene 1.5	Restricted
Vet-Kem Ovitrol Mousse for Cats and Dogs	Wellmark International	22678	(S)-Methoprene = 0.5 Pyrethrins = 0.4 Piperonyl Butoxide = 4.0	Domestic
Zodiac Mousse Flea & Tick Control for Cats and Dogs	Wellmark International	22916	(S)-Methoprene = 0.5 Pyrethrins = 0.4 Piperonyl Butoxide = 4.0	Domestic
Zodiac Premise Plus Flea Spray	Wellmark International	23075	(S)-Methoprene = 0.01 Permethrin = 0.25	Domestic
Vet-Kem Ovicollar for Cats	Wellmark International	23120	(S)-Methoprene = 2.1	Domestic
Vet-Kem Ovicollar for Dogs	Wellmark International	23121	(S)-Methoprene = 1.0	Domestic
Ovex Pump Spray for Dogs and Cats	Wellmark International	23692	(S)-Methoprene = 0.10 Pyrethrins = 0.20 Pieronyl butoxide, technical = 0.37 N-octyl bicycloheptene dicarboximide = 0.62	Domestic
Zodiac Flea Egg Collar for Cats	Wellmark International	23852	(S)-Methoprene = 2.1	Domestic
Zodiac Flea Egg Collar for Dogs	Wellmark International	23853	(S)-Methoprene = 1.0	Domestic

Product Name	Registrant	Registration Number	Guarantee (% a.i.)	Marketing Class
Raid Flea Killer Plus Dog Spray 1	S.C.Johnson & Son Ltd.	24320	(S)-Methoprene = 0.10 Pyrethrins = 0.18 Pieronyl butoxide, technical = 0.36 N-octyl bicycloheptene dicarboximide = 0.60	Domestic
Raid Flea Killer Plus Carpet & Room Spray	S.C.Johnson & Son Ltd.	24580	(S)-Methoprene = 0.015 Pyrethrins = 0.14 Piperonyl butoxide, technical = 1.0 N-octyl bicycloheptene dicarboximide = 1.0 Tetramethrin = 0.064	Domestic
Raid Flea Killer Plus 2 Pressurized Spray	S.C.Johnson & Son Ltd.	24581	(S)-Methoprene = 0.015 Pyrethrins = 0.14 Piperonyl butoxide, technical = 1.0 Tetramethrin = 0.064	Domestic
Hartz Control Pet Care System Flea & Tick Killer for Dogs	Hartz Canada Inc.	24650	(S)-Methoprene = 0.10 Pyrethrins = 0.18 Piperonyl Butoxide Technical = 0.36 N-octyl bicycloheptene dicarboximide = 0.60	Domestic
Hartz Control Pet Care System Home Flea & Tick Killer	Hartz Canada Inc.	24653	(S)-Methoprene = 0.007 Permethrin = 0.25	Domestic
Zodiac Power Band Dual Action Flea & Tick Collar for Cats	Wellmark International	25568**	(S)-Methoprene = 1.02 Tetrachlorvinphos = 14.55	Domestic
Zodiac Power Band Dual Action Flea & Tick Collar for Dogs	Wellmark International	25569**	(S)-Methoprene = 1.02 Tetrachlorvinphos = 14.55	Domestic

Product Name	Registrant	Registration Number	Guarantee (% a.i.)	Marketing Class
Vet-Kem Siphotrol 2000 Double Action Premise Treatment	Wellmark International	25582	(S)-Methoprene = 0.078 Permethrin = 0.80	Domestic
Zodiac Premise 2000 Flea Spray	Wellmark International	25695	(S)-Methoprene = 0.078 Permethrin = 0.80	Domestic
Zodiac Premise 1000 Flea Spray	Wellmark International	25738	(S)-Methoprene = 0.078 Permethrin = 0.80	Domestic
Vet-Kem Siphotrol 1000 Double Action Premise Treatment	Wellmark International	25739	(S)-Methoprene = 0.078 Permethrin = 0.80	Domestic
Hartz Control Pet Care System One Spot – Master	Hartz Canada Inc.	26239	(S)-Methoprene = 2.9 Permethrin = 45	Domestic
Hartz Reference 114 (One Spot) for Cats and Kittens	Hartz Canada Inc.	26255	(S)-Methoprene = 2.9	Domestic
Zodiac Double Action Flea & Tick Shampoo for Dogs and Cats	Wellmark International	26413	(S)-Methoprene = 0.1 Pyrethrins = 0.15 Piperonyl Butoxide = 1.50	Domestic
Hartz Control Pet Care System One Spot for Dogs and Puppies14 kg and Under	Hartz Canada Inc.	26489	(S)-Methoprene = 2.9 Permethrin = 45	Domestic
Hartz Control Pet Care System One Spot for Dogs and Pups over 14 Kg	Hartz Canada Inc.	26490	(S)-Methoprene = 2.9 Permethrin = 45	Domestic
Hartz Control Pet Care System OneSpot Flea Topical Treatment for Cats and Kittens	Hartz Canada Inc.	26491	(S)-Methoprene = 2.9	Domestic

Product Name	Registrant	Registration Number	Guarantee (% a.i.)	Marketing Class
Vet-Kem Ovispot Plus Flea & Tick Control for Dogs Under 14 kg	Wellmark International	26492	(S)-Methoprene = 2.9 Permethrin = 45	Domestic
Zodiac Powerspot Flea & Tick Control for Dogs Over 14 kg	Wellmark International	26493	(S)-Methoprene = 2.9 Permethrin = 45	Domestic
Zodiac Powerspot Flea & Tick Control for Dogs Under 14 kg	Wellmark International	26494	(S)-Methoprene = 2.9 Permethrin = 45	Domestic
Vet Kem Ovispot plus Flea & Tick Control for Dogs over 14 kg	Wellmark International	26495	(S)-Methoprene = 2.9 Permethrin = 45	Domestic
Zodiac Spot On Flea Control for Cats and Kittens	Wellmark International	26496	(S)-Methoprene = 2.9	Domestic
Vet-Kem Ovispot Flea Control for Cats and Kittens	Wellmark International	26497	(S)-Methoprene = 2.9	Domestic
Vet-Kem Ovitrol plus Flea & Tick Shampoo for Dogs and Cats	Wellmark International	26608	(S)-Methoprene = 0.1 Pyrethrins = 0.15 Piperonyl Butoxide = 1.50	Domestic
Apex EC	Wellmark International	27473	(S)-Methoprene = 33.6	Commercial
Altosid XR Briquets	Wellmark International	27694***	(S)-Methoprene = 2.1	Restricted

* Apex EC (Registration No. 17247) is registered as a racemate mixture of S- and R-methoprene with a guarantee of 67% methoprene until 31 December 2008.

** Zodiac Power Band Dual Action Flea & Tick Collar for Cats (Registration No. 25568) and Zodiac Power Band Dual Action Flea & Tick Collar for Dogs (Registration No. 25569) are no longer manufactured, but existing stocks can be used until 27 February 2008, and 6 October 2007, respectively.

*** Altosid XR Briquets (Registration No. 27694) has been granted a temporary registration until 31 December 2006.